UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/838,486	04/07/1997	STEINUNN BAEKKESKOV	02307U-3122	8923

7590 07/29/2003

TOWNSEND AND TOWNSEND AND CREW
TWO EMBARCADERO CENTER 8TH FLOOR
SAN FRANCISCO, CA 941113834

EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	36

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/838,486	Baekkeskov et al.
Examiner	**Art Unit**
G.R. Ewoldt, Ph.D.	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *5/08/03 and 7/22/03*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *31, 35, 49-59, and 62-67* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *31, 35, 49-59, and 62-67* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 31, 35, 49-59, 62, 63, and newly added Claims 64-67 are being acted upon.

2. Applicant's amendment and response, and declarations of Joe Liebeschuetz and Inventor Steinunn Baekkeskov, filed 5/08/03, are acknowledged. The revised "Original executed declaration of Dr. Steinunn Baekkeskov", filed 7/22/03, is acknowledged. Inventor Baekkeskov's 7/22/03 declaration has replaced the 5/08/03 declaration as requested. In view of the instant amendment, the previous rejection of Claims 62 and 63 under the second paragraph of 35 U.S.C. 112 has been withdrawn. Additionally, the previous rejection of Claims 35 and 54-57 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No 4,086,142 has been withdrawn.

3. Applicant's new drawings, filed 5/08/03, have been found acceptable by the Examiner.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 31, 49-53, 58, 62-63, and newly added Claims 64-67 stand/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for inhibiting the development of IDDM in a NOD mouse comprising administering GAD,

does not reasonably provide enablement for:

a method for inhibiting or preventing the development of IDDM in a patient comprising administering GAD, or a fragment thereof,

for the reasons of record set forth in Paper No. 21, mailed 4/21/01 and reiterated in Paper No. 30, mailed 11/04/02.

Note that Claim 59, drawn to a GAD65 composition, was improperly rejected with the method claims in the previous Office action. Said rejection has been withdrawn. Further note that whereas Applicant indicates that "All claims stand rejected for alleged lack of enablement," only the method claims were so rejected.

Applicant's arguments, filed 5/08/03, have been fully considered but have not been found persuasive. Applicant has submitted a declaration of Inventor Baekkeskov in support of the claimed methods.

The Declarant states "When an antigen is administered to a subject, it can induce either a tolerogenic or an immune response depending on the regime with which it is administered. The application teaches that care should be taken not to potentiate an immune response that would exasperate β cell destruction. Based on my knowledge of the scientific literature, general principles for achieving a tolerogenic response rather than a harmful immunogenic response were within the state of the art as of September 1990. For example, standard immunology textbooks available at the priority date of the invention discuss how either low or high dosages of antigen favor a tolerogenic response, whereas intermediate dosages favor an immunogenic response." The Declarant continues "the use of unaggregated antigen favors a tolerogenic response. Induction of antigen specific tolerance had been used successfully in numerous studies to suppress or prevent autoimmune disease in animal models."

The bulk of the jumbo specification discloses the cloning and characterization of the multiple forms of the GAD protein. While routine assays such as ELIAS and RCAS are disclosed in detail, just 2½ pages of the specification are devoted to the pharmaceutical compositions and *in vivo* methods of the instant claims. Applicant felt it necessary to disclose such details as how antibodies are capable of immunoprecipitating GAD, or how rat brain GAD resembles rat β cell GAD, or how GAD_{67} was cloned, yet the Declarant now argues that methods of treating humans, which must be considered orders of magnitude more complex than the mundane tasks of *in vitro* cloning and assaying, "were obtainable based on the teachings of the specification and common knowledge in the field as of September 1990," and therefor not requiring of a detailed description. This position would seem at best, inconsistent. Also note that whereas the Declarant now indicates that high and low dosages, as well as unaggregated antigens, favor a tolerogenic response, these considerations are not disclosed in the specification.

Further regarding the inconsistency of Applicant's arguments, the Examiner previously made of record multiple references, e.g., *Marketleter*, Goodnow, showing that methods of inducing tolerance that worked in animal models have not proved successful in humans; said methods might even be considered dangerous. In the instant response Applicant dismissed the data

stating "Results reported for other diseases are less significant and do nothing to change the undisputed evidence that is directly applicable to insulin dependent diabetes." Yet submitted with the same response, the Declarant argues that numerous results obtained in animal models support the instant methods. It appears then that the Declarant rejects her attorney's position, however, the Declarant has not responded to the fact that while tolerance can be routinely established in animal models, even now, some *13 years* post-filing, the establishment of tolerance in humans cannot be considered to be routine. The Declarant has even cited the work of Weiner et al. in support of the instant invention. It must be noted however, that this is the very work cited by the Examiner as functioning in the animal model yet proving to be a complete failure in humans. It is unclear how this work can be seen as supporting the method of the instant claims. The best the Declarant can provide are preliminary results achieved in a related pathology of non-autoimmune origin (type II diabetes). Regarding said results, they contain no teaching of the use of only high or low dosages of GAD as would be expected to be required given the Declarant's instant arguments. Accordingly, the Declarant's assertion that the establishment of tolerance in humans would have been routine in September 1990 appears to fly in the face of scientific reality.

The Declarant argues that the NOD mouse is a good model for IDDM and that in many ways it is superior to the BB rat model.

It is the Examiner's position that while the NOD mouse model may be the best available model, the use of said model still comprises little more than the equivalent of a single case study. And it is again noted that the specification discloses no use of this model in establishing the efficacy of the claimed method. Thus, it remains the Examiner's position that some 13 years post-filing, even with the available NOD mouse model results, tolerance-inducing therapies developed employing said model have not translated into effective human therapies for the treatment of IDDM. Accordingly said therapies could not have been considered to be routine in 1990 employing only the brief teachings of the instant specification.

Finally, it is noted that Applicant has not responded to the rejection based on the recitation of "fragment" in the instant claims.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled requirements of paragraphs (1), (2), and (4) of section 3c of this title before the invention thereof by the applicant for patent.

7. Claim 31 and newly added Claims 64 and 65, stands/are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,762,937 (of record), for the reasons of record as set forth in Papers No. 21 and 30, mailed 4/24/01 and 11/04/02, respectively.

Applicant has requested an interference be established. Applicant is advised that the establishment of an interference will not be considered nor commented upon until such time as all pending claims are in condition for allowance. Applicant has additionally requested clarification as to whether the claim is rejected over the claims or the specification. A set forth in Paper No. 21, the claim is rejected over both the claims and the specification.

8. Claims 35, 49, and 54-57 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by U.S. Patent No 5,762,937, for the reasons of record set forth in Paper No. 30, mailed 11/04/02.

Applicant's arguments, filed 5/08/03, have been fully considered but have not been found persuasive. Applicant argues that the rejection can only be overcome by interference as it is assumed that the rejection is based on the claims. Applicant is advised that the rejection pointed particularly to Example 14, thus, indicating that the rejection was based not solely on the claims but also on the teachings of the specification in which the lower molecular weight antigen (the 64KA antigen) is referred to repeatedly.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 50-53, 58-59, and newly added Claims 66 and 67, stand/are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No 5,762,937.

Applicant's arguments, filed 5/08/03, have been fully considered but have not been found persuasive. Applicant argues that the rejection can only be overcome by interference as it is assumed that the rejection is based on the claims. Applicant is advised that the rejection pointed particularly to Example 14, thus, indicating that the rejection was based not solely on the claims but also on the teachings of the specification in which the lower molecular weight antigen (the 64KA antigen) is referred to repeatedly.

11. The following are new grounds for rejection necessitated by Applicant's amendment.

12. Claims 35 and 54-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No 4,086,142 in view of U.S. Patent No 4,736,020.

the '142 patent teaches a composition in a pharmaceutically acceptable carrier comprising GAD (see particularly, column 4, lines 14-16). Note that GAD comprises the same chemical composition regardless of source.

The reference teaching differs from the invention of the instant claims only in that the composition of the reference is not at least 99% w/w/ pure.

The '020 patent teaches the purification of a polypeptide to a purity of at least 99% (see particularly Examples 1, 3, and 5).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a GAD that was at least 99% w/w/pure, as taught by the combined '142 and '020 patents. One of ordinary skill in the art at the time the invention was made would have been motivated to produce said purified polypeptide as the purification of polypeptides to said purity was well-known in the art and it would generally be considered more preferable to use more pure reagents. Thus, the addition of a new limitation to the claims requiring 99% purity of the claimed GAD polypeptide does not render the invention of the instant claims patentably distinct.

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600
July 28, 2003